LACHMAN CONSULTANT SERVICES, INC.
CONSULTANTS TO THE PHARMACEUTICAL AND ALLIED INDUSTRIES

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April 6, 2000

Dockets Management Branch
Food and Drug Administration (HFA-305)
5630 Fishers Lane
Room 1061
Rockville, MD 20852

**In Quadruplicate**

## CITIZEN PETITION

Pursuant to 21 CFR 10.20 and 10.30, Lachman Consultant Services, Inc. (LCS), is submitting this petition in quadruplicate under Section 505 (j)(2)(C) of the Federal Food, Drug and Cosmetic Act to request that the Commissioner of Food and Drugs make a determination that an Abbreviated New Drug Application may be submitted for Nizatidine Capsules, 75 mg.

### A. Action Requested

The petitioner requests that the Commissioner of the Food and Drug Administration make a determination that Nizatidine Capsules, 75 mg, are suitable for submission as an Abbreviated New Drug Application. The reference-listed drug product upon which this petition is based is Axid AR Tablets, 75 mg (Whitehall Robins Healthcare). Lachman Consultant Services, Inc., seeks a change in dosage form from that of the reference-listed drug product to include a capsule dosage form.

### B. Statement of Grounds

The Federal Food, Drug and Cosmetic Act provides for the submission of an Abbreviated New Drug Application for a new drug that differs in dosage form from a listed drug provided the FDA has approved a petition that proposed the filing of such an application. This petition involves a change in the dosage form for the proposed drug from that of the listed drug. The listed drug on which this petition is based is manufactured by Whitehall Robins Healthcare. The listing of Axid AR Tablets is on page 3-349 of the Nineteenth Edition of the Approved Drug Products with Therapeutic Equivalence Evaluations (Attachment I).

The reference-listed drug (RLD) product is a tablet dosage form containing 75 mg of Nizatidine. The RLD is marketed as an over-the-counter (OTC) product. The proposed capsule drug product represents the same strength and same active ingredient as the reference-listed drug.

In support of this proposed change, we refer to the numerous OTC products are marketed in both tablet and capsule dosage forms. Alternate dosage forms offer

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users an option for those patients who may have difficulty in swallowing a tablet or prefer a capsule dosage form. The petitioner is seeking this change in dosage form to provide such an alternative to individuals who prefer a capsule dosage form. The Agency has previously approved ANDA suitability petitions allowing for a change in dosage form (from a tablet to a capsule) in many instances. Additionally, the prescription strengths of Axid Pulvules, 150 mg and 300 mg (Nazitidine) are currently marketed as a capsule dosage form. There are no proposed changes in labeling with the exception of the required change due to the change in dosage form sought in this petition.

In accordance with the Regulations Requiring Manufacturers to Assess the Safety and Effectiveness of New Drugs and Biological Products in Pediatric Patients; Final Rule (Pediatric Rule) published December 2, 1998, the petitioner claims the following.

The approved labeling for the reference–listed drug states that the product should not be given to children under 12 years old unless directed by a physician. Nizatidine appears on the Agency's list of approved drugs for which additional pediatric information may produce health benefits in the pediatric population. The indication cited on this list is "erosive esophagitis". The approved labeling for the reference-listed drug states that Nizatidine Tablets, 75 mg, are used to prevent heartburn, acid indigestion and sour stomach brought on by consuming food and beverages. Erosive esophagitis is not an approved indication for the over-the-counter product. The regulations (21 CFR 314.55) state that each application for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration shall contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric sub-populations, and to support dosing and administration for each pediatric sub-population for which the drug is safe and effective. The proposed product does not include a claimed indication for which the Agency is seeking additional pediatric information, that is, the over-the-counter product does not contain the labeled indication of erosive esophagitis. Therefore, the petitioner certifies its belief that the requested change in dosage form (from a tablet to a capsule) does not represent a meaningful therapeutic benefit over existing therapies for the age group that is not already covered in the existing labeling. The petitioner does not believe that a change in dosage form from a tablet to a capsule will result in any additional usage in the existing pediatric population for which the product is currently approved. Therefore, the petitioner requests a waiver under 21 CFR 201.23 for the need to conduct pediatric studies for the proposed change in dosage form.

A copy of the reference-listed drug labeling is included as Attachment II and draft labeling for the proposed Nizatidine Capsules is included as Attachment III. The

uses, dosage and indications for the proposed product are the same as those for Axid AR Tablets, the reference-listed drug.

## C. Environmental Impact

An environmental assessment on the action requested in this petition qualifies for a categorical exclusion under 21 CFR 25.24 (c)(1) as provided for in 21 CFR 25.23 (c). Therefore, an environmental assessment is not required for the requested action.

## D. Economic Impact

Pursuant to 21 CFR 10.30 (b), economic impact information is to be submitted only when requested by the Commissioner. LCS will promptly provide such information if so requested.

## E. Certification

LCS certifies that, to its best knowledge and belief, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Respectfully submitted,

Gordon Johnston

Gordon Johnston
Associate

GJ/pf

Attachments: Listing of reference listed drug; Approved Drug Products with Therapeutic Equivalence Ratings, Nineteenth Edition
Labeling for Reference Drug
Draft Labeling for Proposed Drug

cc: G. Davis (OGD)
L. Lachman
R Pollock

*66k0096*

NAPROXEN SODIUM

TABLET; ORAL

| | | | |
|---|---|---|---|
| ALEVE | | | |
| + BAYER | EQ 200MG BASE | N20204 002 | JAN 11, 1994 |
| NAPROXEN SODIUM | | | |
| GRANUTEC | EQ 200MG BASE | N74635 001 | JAN 13, 1997 |
| INVAMED | EQ 200MG BASE | N74646 001 | JAN 13, 1997 |
| PAR PHARM | EQ 200MG BASE | N75168 001 | JUL 28, 1998 |
| PERRIGO | EQ 200MG BASE | N74661 001 | JAN 13, 1997 |
| PVT FORM | EQ 200MG BASE | N74789 001 | FEB 27, 1997 |

NEOMYCIN SULFATE; *MULTIPLE*
SEE BACITRACIN ZINC; NEOMYCIN SULFATE; POLYMYXIN B SULFATE

NICOTINE

FILM, EXTENDED RELEASE; TRANSDERMAL

| | | | |
|---|---|---|---|
| NICODERM CQ | | | |
| + HOECHST MARION RSSL | 7MG/24HR | N20165 006 | AUG 02, 1996 |
| + | 14MG/24HR | N20165 005 | AUG 02, 1996 |
| + | 21MG/24HR | N20165 004 | AUG 02, 1996 |
| NICOTROL | | | |
| + PHARMACIA AND UPJOHN | 15MG/16HR | N20536 001 | JUL 03, 1996 |

NICOTINE POLACRILEX

GUM, CHEWING; BUCCAL

| | | | |
|---|---|---|---|
| NICORETTE | | | |
| + SMITHKLINE BEECHAM | EQ 2MG BASE | N18612 002 | FEB 09, 1996 |
| + | EQ 4MG BASE | N20066 002 | FEB 09, 1996 |
| NICORETTE (MINT) | | | |
| + SMITHKLINE BEECHAM | EQ 2MG BASE | N18612 003 | DEC 23, 1998 |

NICOTINE POLACRILEX

GUM, CHEWING; BUCCAL

| | | | |
|---|---|---|---|
| NICORETTE (MINT) | | | |
| + SMITHKLINE BEECHAM | EQ 4MG BASE | N20066 003 | DEC 23, 1998 |

NIZATIDINE

TABLET; ORAL

| | | | |
|---|---|---|---|
| AXID AR | | | |
| + WHITEHALL ROBINS | 75MG | N20555 001 | MAY 09, 1996 |

OCTYL METHOXYCINNAMATE; *MULTIPLE*
SEE AVOBENZONE; OCTYL METHOXYCINNAMATE; OXYBENZONE

OXYBENZONE; *MULTIPLE*
SEE AVOBENZONE; OCTYL METHOXYCINNAMATE; OXYBENZONE

OXYMETAZOLINE HYDROCHLORIDE

SOLUTION/DROPS; OPHTHALMIC

| | | | |
|---|---|---|---|
| OCUCLEAR | | | |
| SCHERING PLOUGH | 0.025% | N18471 001 | MAY 30, 1986 |
| VISINE L.R. | | | |
| + PFIZER | 0.025% | N19407 001 | MAR 31, 1989 |

PERMETHRIN

LOTION; TOPICAL

| | | | |
|---|---|---|---|
| NIX | | | |
| + WARNER LAMBERT | 1% | N19918 001 | MAY 02, 1990 |

PHENIRAMINE MALEATE; *MULTIPLE*
SEE NAPHAZOLINE HYDROCHLORIDE; PHENIRAMINE MALEATE

PHENYLPROPANOLAMINE HYDROCHLORIDE; *MULTIPLE*
SEE BROMPHENIRAMINE MALEATE; PHENYLPROPANOLAMINE HYDROCHLORIDE
SEE CHLORPHENIRAMINE MALEATE; PHENYLPROPANOLAMINE HYDROCHLORIDE

PDR for Nonprescription Drugs® entry for
**Axid AR Tablets** (Whitehall-Robins)

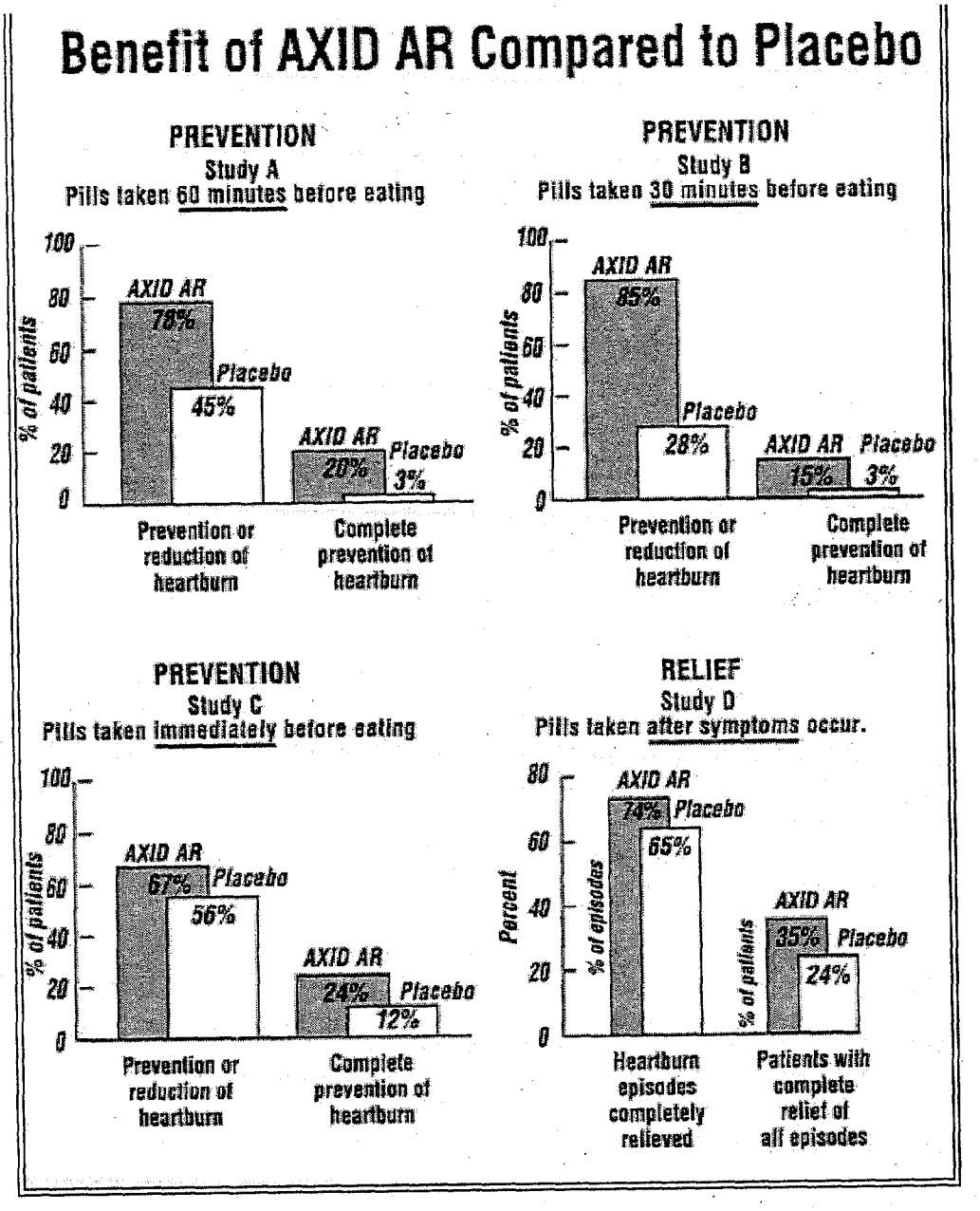
**Active Ingredient:** Nizatidine 75 mg per tablet.

**Inactive Ingredients:** Colloidal Silicon Dioxide, Hydroxypropylmethylcellulose, Synthetic Iron Oxides, Magnesium Stearate, Microcrystalline Cellulose, Polyethylene Glycol, Pregelatinized Starch, Propylene Glycol, Corn Starch, Titanium Dioxide.

**Product Benefits:** Taken right before eating or up to 60 minutes before eating, one tablet of AXID® AR prevents heartburn, acid indigestion, and sour stomach caused by food and beverages. Unlike antacids which neutralize acid after symptoms have occurred, AXID AR reduces the production of acid in the stomach so you can prevent symptoms. AXID AR also relieves heartburn, acid indigestion and sour stomach.

**Action:** The stomach normally produces acid especially following eating and drinking. Sometimes, acid backing up into the esophagus can cause a burning pain and discomfort, commonly known as heartburn.

**In clinical studies AXID AR was significantly better than placebo in preventing and relieving heartburn symptoms.**




**Use:** For relief and/or prevention of heartburn, acid indigestion and sour stomach brought on by consuming food and beverages.

**How to help avoid symptoms:**

- Avoid lying down flat or bending over soon after eating.
- Avoid eating late at night or right before bedtime.
- If you are overweight, lose weight.
- If you smoke, stop or cut down.
- Eat slowly and do not eat big meals.
- Elevate the head of your bed
- Avoid wearing tight fitting clothing around your stomach.

- Avoid certain foods or beverages more likely to cause heartburn, such as rich, spicy, fried foods, chocolate, caffeine, alcohol; even some fruits and vegetables.

**Warnings:** While the symptoms of heartburn are common, you should see your doctor promptly if:

- You have trouble swallowing or persistent abdominal pain. You may have a serious condition that may need different treatment.
- You have taken the maximum dosage (2 tablets per 24 hours) for 2 weeks continuously.

**Important:**

- As with any drug, if you are pregnant or nursing a baby, seek the advice of a health professional before using this product.
- This product should not be given to children under 12 years old unless directed by a doctor.
- Keep this and all drugs out of the reach of children.
- In case of accidental overdose, seek professional assistance or contact a poison control center immediately.

**Directions:** To prevent heartburn, take one tablet with a full glass of water right before eating or up to 60 minutes before consuming food and beverages that you expect to cause symptoms. For relief of symptoms, take one tablet with a full glass of water. AXID AR can be used up to twice daily (up to 2 tablets in 24 hours); the maximum daily dosage.

**How Supplied:** AXID AR Acid Reducer is available in boxes of 6 individual packets and bottles of 12, 18, 30, and 50 tablets.

Store at 20°-25° C (68°-77°F). Protect from light. Replace cap tightly after opening bottle. The bottle is sealed with printed foil under cap. Do not use if foil is open or torn.

LACHMAN CONSULTANT SERVICES, INC.
Westbury, NY 11590

## DRAFT LABELING

Nizatidine Capsules, 75 mg

**Active Ingredient:** Nizatidine 75 mg per capsule

**Inactive Ingredient**: To be listed.

**Product Benefits**: Taken right before eating or up to 60 minutes before eating, one capsule of Nizatidine 75 mg prevents heartburn, acid indigestion, and sour stomach caused by food and beverages. Unlike antacids which neutralize acid after symptoms have occurred, Nizatidine Capsules reduces the production of acid in the stomach so you can prevent symptoms, Nizatidine Capsules also relieves heartburn, acid indigestion and sour stomach.

**Action**: The stomach normally produces acid especially following eating and drinking. Sometimes, acid backing up into the esophagus can cause a burning pain and discomfort, commonly known as heartburn.

**In clinical studies, Nizatidine Capsules were significantly better than placebo in preventing and relieving heartburn symptoms.**

**Use**: For relief and/or prevention of heartburn, acid indigestion and sour stomach brought on by consuming food and beverages.

**How to help avoid symptoms:**

- Avoid lying down or bending over soon after eating.
- Avoid eating late at night or right before bedtime.
- If you are overweight, lose weight.
- If you smoke, stop or cut down.
- Eat slowly and do not eat big meals.
- Elevate the head of your bed.
- Avoid wearing tight fitting clothing around your stomach.
- Avoid certain foods or beverages more likely to cause heartburn, such as rich, spicy, fried foods, chocolate, caffeine, alcohol; even some fruits and vegetables.

**Warnings:** While the symptoms of heartburn are common, you should see your doctor promptly if:

- You have trouble swallowing or persistent abdominal pain. You may have a serious condition that may need different treatment.
- You have taken the maximum dosage (2 Capsules per 24 hours) for 2 weeks continuously.

**Important**:

- As with any drug, if you are pregnant or nursing a baby, seek the advice of a health professional before using this product.
- This product should not be given to children under 12 years old unless directed by a doctor.
- Keep this and all drugs out of the reach of children.
- In case of accidental overdose, seek professional assistance or contact a poison control center immediately.

**Directions**: To prevent heartburn, take one tablet with a full glass of water right before eating or up to 60 minutes before consuming food and beverages that you expect to cause symptoms. For relief of symptoms, take one tablet with a full glass of water. Nizatidine Capsules can be used up to twice daily (up to 2 Capsules in 24 hours); the maximum daily dosage.

**How Supplied**: Nizatidine Capsules, 75 mg, are available in boxes of 6 individual packets and bottles of 12, 18, 30, and 50 Capsules.

Store at 20° – 25°C (68° – 77°F). Protect from light. Replace cap tightly after opening bottle. The bottle is sealed with printed foil under cap. Do not use if foil is open or torn.

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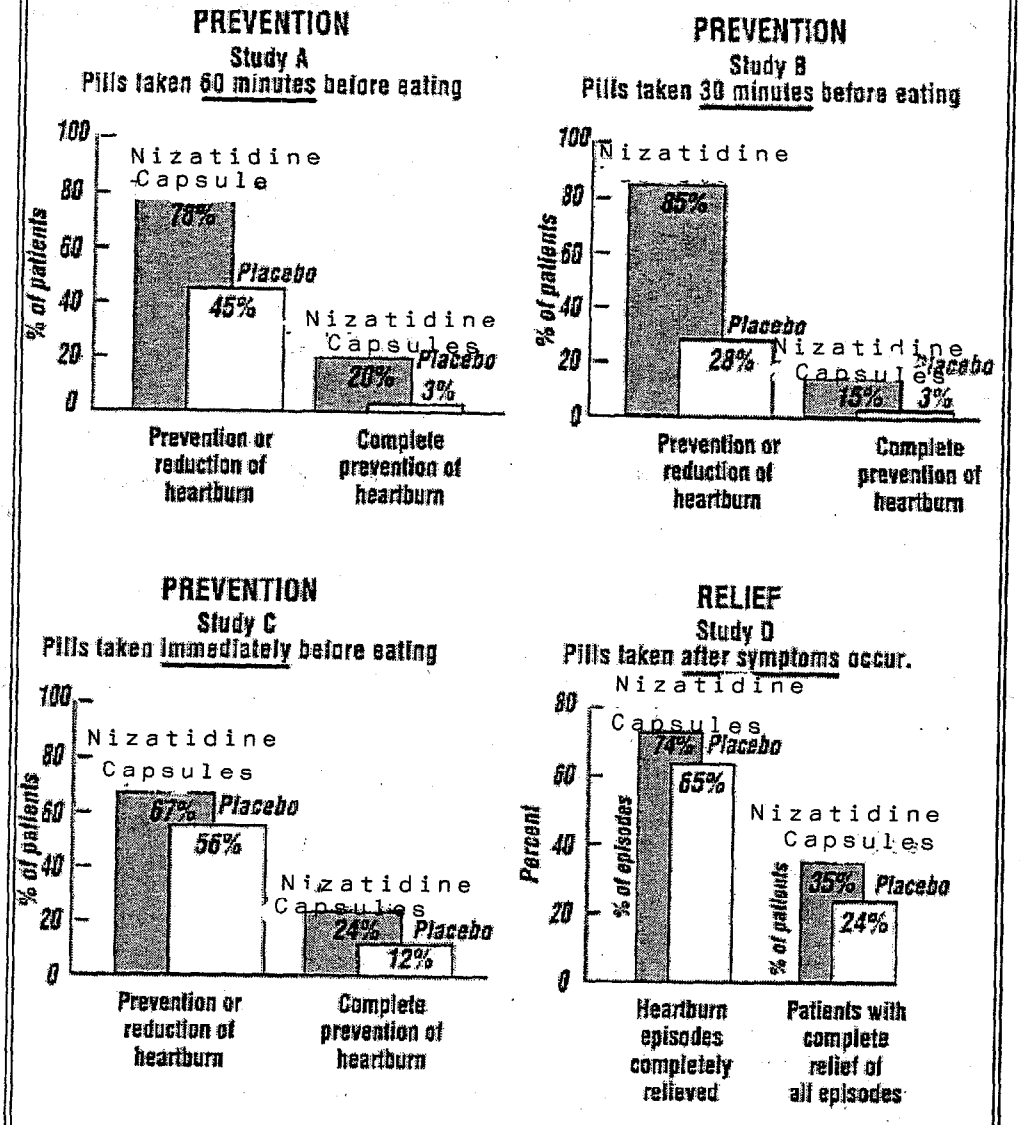
## Benefit of Nizatidine Capsules Compared to Placebo



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